

REMARKS

Claims 32-70 are pending. Claims 33-35 and 48-70 are withdrawn from consideration. Claims 32 and 36-47 are under consideration.

Applicants submit these remarks in response to the Office Action (non-final rejection) dated March 14, 2005 ("Office Action"). Applicants have also filed a one-month Petition for Extension of time and believe that this extension of time is effective to allow timely filing of a response up to and including July 14, 2005. In the event that Applicants are incorrect in their assumption, please charge any fee due in connection with this submission to Deposit Account No.23-2415 referencing docket no. 30923-703.301. Accordingly, entry of the amendments and consideration of the comments is proper and is respectfully requested.

Claim 31 has been cancelled without prejudice or disclaimer of the subject matter recited therein and the features thereof have been incorporated in Claims 32. As all of the amendments are supported by the original disclosure and claims, no new matter has been added. The above amendments should not be construed as constituting any admission with respect to the patentability of the previously claimed subject matter, and Applicants reserve the right to pursue the cancelled subject matter in one or more continuing patent applications.

*Interview Summary*

Applicants thank Examiner Celsa for the courteous Telephonic Examiner Interview ("Interview") conducted on June 28, 2005. Applicants' representatives Tobey Tam and Samir Elamrani wish to express their appreciation for the helpful comments provided by the Examiner during the Interview. A summary of the substance of the Interview is provided below.

In the Interview, Applicants' representatives explained how the invention as set forth in Claim 31 satisfies fully the written description and enablement requirements of 35 U.S.C. § 112 ¶1. Applicants representatives also pointed to the features that distinguish the invention as claimed from the documents relied upon in the art rejections set forth in the Office Action.

Applicants' representatives also indicated that they will consider canceling Claim 31 for the sole purpose of expediting the prosecution of the subject application while reserving the right to pursue the full scope of that claim in a future continuation application. The Examiner indicated that he was favorably inclined to consider Applicants' amendments and comments.

Consistent with the discussions during the interview, Applicants have amended the application by canceling Claim 31 and amending Claim 32 to read as an independent claim. Rewriting Claim 32 in independent form does not change the scope of this claim and should therefore introduce no new issues. Applicants' remarks provided below are believed to be consistent with the discussions with the Examiner. Accordingly, it is believed that in light of the above amendments to the claims and the remarks provided below, the application is in condition for allowance and such favorable action is earnestly solicited.

**Claim Amendments**

Claim 31 has been cancelled without prejudice or disclaimed to the subject matter recited therein. Claim 32 has been rewritten in independent form by amending the claim to incorporate the features of Claim 31.

**The Rejection of Claim 31 Under 35 U.S.C. § 112 ¶1**

In the Office Action, Claim 31 was rejected Under 35 U.S.C. § 112 ¶1 as allegedly failing to comply with the written description requirement (pages 3-6 of the Office Action). Claim 31 was also rejected under 35 U.S.C. § 112 ¶1 for alleged lack of enabling specification (pages 6-9 of the Office Action). By the above amendments, Claim 31 has been cancelled in order to expedite prosecution of the subject application. Accordingly, it is believed that the rejections under 35 U.S.C. § 112 ¶1 have been obviated. Thus, withdrawal of the rejections is in order and is respectfully requested.

**The Rejection of Claim 31 Under 35 U.S.C. § 102**

In the Office Action, Claim 31 was rejected Under 35 U.S.C. § 102 as allegedly being anticipated by Francoeur, U.S. Patent No. 4,880,750 (*Francoeur*). As explained during the

Interview, Applicants disagree with the assertion in the Office Action as *Francoeur* fails to disclose each of the features recited in Claim 31. However, in order to expedite prosecution of the subject application, and consistent with the discussions during the Interview, Claim 31 has been cancelled. Accordingly, the rejection based on *Francoeur* has been rendered moot and withdrawal of the rejection is respectfully requested.

**The Rejection of Claims 31, 32, 36-45 and 47 Under 35 U.S.C. § 102**

Claims 31, 32, 36-45 and 47 were rejected Under 35 U.S.C. § 102 as allegedly being anticipated by *Morton et al.* Biochem. Vol. 34, No. 27 (1995) pages 8564-8575 (*Morton et al.*). Again consistent with the discussion during the Interview and in order to expedite allowance of the subject application, Claim 31 has been cancelled and Applicants reserve the right to pursue the subject matter thereof in a continuation application. Accordingly, the rejection of Claim 31 based on *Morton et al.* has been rendered moot and withdrawal thereof is respectfully requested. Moreover, for at least the reasons discussed during the interview and further summarized below, Applicants traverse the rejection based on *Morton et al.* in as much as it is applied to Claims 32, 36-45 and 47.

As defined by Claim 32, the present invention relates to a method for determining at least one previously unidentified biological function of a target protein comprising: (a) screening a multiplicity of different molecules for their ability to modify the stability of a target protein, wherein modification of the stability of said target protein by a molecule indicates that the molecule binds to said target protein; (b) generating, from step (a), a first list of molecules that modify the stability of said target protein; (c) comparing said first list from step (b) to at least one second list of molecules, wherein said second list of molecules are known to modify the stability of a group of proteins which share biological function; and (d) determining if any molecule in said first list from step (b) is included in said second list from step (c), thereby determining at least one previously unidentified biological function of said target protein. As further recited in Claim 32, step (a) comprises: (a1) contacting said target protein with one or more of said multiplicity of different molecules in each of a multiplicity of containers; (a2) treating said target

protein in each of said multiplicity of containers to cause said target protein to unfold; (a3) measuring in each of said containers a physical change associated with the unfolding of said target protein; (a4) generating an unfolding curve for said target protein for each of said containers; (a5) comparing each of said unfolding curves in step (a4) to (1) each of said other unfolding curves and to (2) the unfolding curve obtained for said target protein in the absence of any of said multiplicity of different molecules; and (a6) determining whether any of said multiplicity of different molecules modifies the stability of said target protein, wherein a modification in stability is indicated by a change in said unfolding curve.

*Morton et al.* cannot not fairly anticipate the present invention. *Morton et al.* does not suggest, much less disclose each feature of Claims 32, 36-45 or 47. For example, *Morton et al.* does not disclose step (d) determining if any molecule in said first list from step (b) is included in said second list from step (c), thereby determining at least one previously unidentified biological function of said target protein. In fact *Morton et al.* is not concerned at all with determining unknown biological function of a target protein.

*Morton et al.* relates to determining the interactions within the core of a folded protein by analyzing the binding of different compounds to an internal cavity in the interior of phage T4 lysozyme by site directed mutagenesis. The binding energetics were analyzed by dividing the reaction into three processes: desolvation, immobilization, and packing. The analysis purportedly indicates that all three processes contribute to binding specificity. (See Abstract).

That *Morton et al.* is directed to the identification of the contribution of various energetic factors to protein bindings is apparent throughout the document. For example, in the paragraph bridging pages 8569 and 8570 it is stated that:

“Many studies have shown that the substitution of one type of amino acid for another in the core of a protein can have different consequences for protein stability, depending on the particular site of substitution [e.g., Shortle et al. (1990) and Eriksson et al. (1992b)]. This is because in addition to the hydrophobic effect

context-dependent steric interactions and entropic effects are also important. The contributions of effects other than hydrophobicity have also been seen in studies of protein-ligand interactions (Estell et al., 1986; Bigler et al., 1993). The work described here attempts to experimentally separate these effects from one another and from other factors such as hydrogen bonding and salt bridge formation. In particular, we try to estimate the energetic contributions arising from packing effects and from configurational and conformational statistics relative to contribution from solvent transfer." Emphasis added

*Morton et al.* does not attempt to determine an unknown function of lysozyme, much less determine such function using the method presently claimed. As apparent from the section above and the document in general, *Morton et al.* simply uses lysozyme (a protein of well known function) as a system for separating energetic components such as energetic contributions arising from packing effects and from configurational and conformational statistics relative to contribution from solvent transfer. There is simply no disclosure whatsoever in *Morton et al.* of a method for determining at least one previously unidentified biological function of a target protein (lysozyme) comprising (b) generating, from step (a), a first list of molecules that modify the stability of said target protein; (c) comparing said first list from step (b) to at least one second list of molecules, wherein said second list of molecules are known to modify the stability of a group of proteins which share biological function; and (d) determining if any molecule in said first list from step (b) is included in said second list from step (c), thereby determining at least one previously unidentified biological function of said target protein.

Thus, *Morton et al.* cannot and does not anticipate the present claims. Accordingly the rejection based on *Morton et al.* should be withdrawn and such action is respectfully requested.

**The Rejection of Claims 31, 32, 36-45 and 47 Under 35 U.S.C. § 103(a)**

Claims 31, 32, and 36-47 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Pantoliano et al. U.S. Patent No. 6,020,141 and Kauvar WO 95/18969. The

Office Action alleges on pages 18 and 19 that the claims are obvious over the combination of Pantoliano et al and Kauvar. This rejection is traversed for at least the following reasons.

As discussed during the Interview U.S. Patent No. 6,020,141 and the subject application are commonly owned. As indicated by the attached filing receipt, the subject application is a continuation of U.S. Application No. 09/190,128 (filed on November 12, 1998. Claiming priority to U.S. Provisional Application No. 60/065,129 filed November 12, 1997). As indicated by the attached recorded assignment (Reel/Frame 9859/0371) U.S. Application 09/190,128 and continuations therefrom are assigned to 3-Dimensional Pharmaceuticals, Inc. (now part of Johnson & Johnson PRD). Likewise, the attached recorded assignment (Reel/Frame 8978/0050) indicates that U.S. Application 08/853,464 now U.S. Patent No. 6,020,141 is also assigned to 3-Dimensional Pharmaceuticals, Inc. Accordingly, the conditions set forth in MPEP Section 706.02(I)(3), are satisfied and U.S. Patent No. 6,020,141 is properly disqualified as prior art under § 103(a) against the subject application.

Thus, withdrawal of the rejection under 35 U.S.C. § 103(a) based on U.S. Patent No. 6,020, 141 in combination with Kauvar is in order and such favorable action is respectfully requested.

CONCLUSION

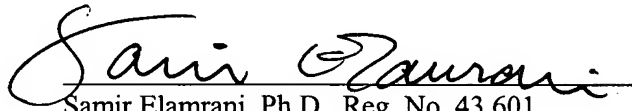
Applicants respectfully request favorable action in the form of an allowance of Claims 32 and 36-47. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (858) 350-2337.

Respectfully submitted,

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